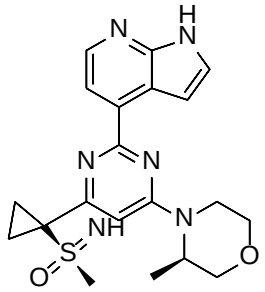
Product data sheet

MedKoo Cat#: 206114 Name: Ceralasertib CAS#: 1352226-88-0 (free base) Chemical Formula: $C_{20}H_{24}N_6O_2S$ Exact Mass: 412.1682 Molecular Weight: 412.51	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Ceralasertib, also known as AZD6738, is an orally available morpholino-pyrimidine-based inhibitor of ataxia telangiectasia and rad3 related (ATR) kinase, with potential antineoplastic activity. Upon oral administration, ATR kinase inhibitor Ceralasertib selectively inhibits ATR activity by blocking the downstream phosphorylation of the serine/threonine protein kinase CHK1. This prevents ATR-mediated signaling, and results in the inhibition of DNA damage checkpoint activation, disruption of DNA damage repair, and the induction of tumor cell apoptosis.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	60.5	146.67
Ethanol	83.0	201.21

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.42 mL	12.12 mL	24.24 mL
5 mM	0.48 mL	2.42 mL	4.85 mL
10 mM	0.24 mL	1.21 mL	2.42 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Min A, Im SA, Jang H, Kim S, Lee M, Kim DK, Yang Y, Kim HJ, Lee KH, Kim JW, Kim TY, Oh DY, Brown J, Lau A, O'Connor MJ, Bang YJ. AZD6738, A Novel Oral Inhibitor of ATR, Induces Synthetic Lethality with ATM Deficiency in Gastric Cancer Cells. Mol Cancer Ther. 2017 Apr;16(4):566-577. doi: 10.1158/1535-7163.MCT-16-0378. Epub 2017 Jan 30. PMID: 28138034.

In vivo study

1. Min A, Im SA, Jang H, Kim S, Lee M, Kim DK, Yang Y, Kim HJ, Lee KH, Kim JW, Kim TY, Oh DY, Brown J, Lau A, O'Connor MJ, Bang YJ. AZD6738, A Novel Oral Inhibitor of ATR, Induces Synthetic Lethality with ATM Deficiency in Gastric Cancer Cells. Mol Cancer Ther. 2017 Apr;16(4):566-577. doi: 10.1158/1535-7163.MCT-16-0378. Epub 2017 Jan 30. PMID: 28138034.

7. Bioactivity
Biological target: Ceralasertib (AZD6738) is an inhibitor of ATR kinase with an IC50 of 1 nM.

In vitro activity

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To assess the antiproliferative activity of AZD6738 (a novel ATR inhibitor), its growth-inhibitory effects were investigated in 14 gastric cancer cell lines using an MTT assay. In sensitive SNU-601 cells, ATR inhibition dose-dependently induced the downregulations of proliferative signaling molecules, including AKT, STAT3, and ERK (Fig. 1A). The S and sub-G1 populations of SNU-601 cells were dramatically and dose-dependently increased by AZD6738 (Fig. 1B), and increased levels of cleaved PARP and caspase-3 along with γ-H2AX expression were consistent with FACS data. Inhibition of cell-cycle progression by AZD6738 also led to the downregulation of thymidylate synthase (TS), cyclin E, and p21 expression in SNU-601 cells (Fig. 1C).

Reference: Mol Cancer Ther. 2017 Apr;16(4):566-577. https://mct.aacrjournals.org/content/16/4/566.long

In vivo activity

To determine whether inhibition of ATR effectively inhibits in vivo tumor growth, a SNU-601 xenograft model was utilized. The tumor volumes in mice administered AZD6738 (50 mg/kg daily) were significantly smaller than in vehicle control (Fig. 5A), and at this dose, AZD6738 was well tolerated (Fig. 5B). Furthermore, Ki-67 expression (an indicator of proliferation) was lower in AZD6738-treated mice than in nontreated controls, indicating lower proliferative ability in AZD6738 treated mice, and TUNEL assay showed AZD6738 also increased numbers of apoptotic cells (Fig. 5C). These findings reinforce the notion that ATR inhibition significantly suppresses cell proliferation and promotes apoptosis in vivo.

Reference: Mol Cancer Ther. 2017 Apr;16(4):566-577. https://mct.aacrjournals.org/content/16/4/566.long